

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
**(Attorney Docket No. 01-1081)**

<b>In the Application of:</b>	)	
	)	
<b>GRAF et al.</b>	)	
	)	<b>Examiner: Vanessa L. Ford</b>
<b>Serial No.: 09/937,103</b>	)	
	)	<b>Group Art Unit: 1645</b>
<b>Filing Date: July 5, 2002</b>	)	
	)	<b>Confirmation No.: 4719</b>
<b>For: Use of Trehalose For Stabilizing</b>	)	
<b>A Liquid Vaccine</b>	)	

Mail Stop Appeal Brief- Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**APPLICANTS' REPLY TO EXAMINER'S ANSWER**

Dear Sir:

Please consider the following remarks in reply to the Examiner's Answer.

The Examiner's Answer states that it relies upon the prior art teaching that trehalose stabilizes macromolecules against thermal inactivation:

1. "Sola-Penna *et al.* teach that trehalose is the best stabilizer of macromolecules because trehalose has the ability to protect these molecules from thermal inactivation (see the Abstract)." Examiner's Answer, p. 4, ll. 13-15.
2. "The prior art also teaches that trehalose is the most effective non-reducing sugar in stabilizing pharmaceutical compositions and protecting them from thermal inactivation." Examiner's Answer, p. 9, ll. 14-16.
3. "...it should be noted that the combination of prior art references teach that trehalose is effective in protecting enzymes (antigens) from thermal inactivation." Examiner's Answer, p. 10, ll. 6-8.

However, none of the prior art provides any teachings that would lead one of ordinary skill to infer that the decrease of immunogenicity of a polysaccharide-protein conjugate antigen in a liquid vaccine is due to thermal inactivation. Simply put, the prior art does not recognize a connection between (a) thermal stability and (b) immunogenicity of polysaccharide-protein conjugates.

Without the recognition of such a connection there would be no reason for one of ordinary skill in the art to combine a thermal degradation stabilizing agent such as trehalose with an immunogenic polysaccharide-protein conjugate antigen in a liquid vaccine. There is nothing in the prior art from which one of ordinary skill could infer any apparent advantage that would be obtained by such a combination.

The prior art only teaches that trehalose aids in preventing thermal inactivation of enzymatic activity. But the polysaccharide-protein conjugates recited in the present claims do not act enzymatically in the recited liquid vaccine compositions. Thus, there is no enzymatic activity to maintain or enhance. One would not seek to use an additive to maintain/enhance a desirable property of a compound if the compound does not possess that property. As the polysaccharide-protein conjugate does not act enzymatically, there is no reason to add an agent such as trehalose that is intended to maintain enzymatic activity.

For these reasons as well as the reasons presented in their Appeal Brief, the applicants respectfully submit that this rejection is improper and request that it be withdrawn.

Respectfully submitted,

Date: January 18, 2007

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